

AMENDMENTS TO THE SPECIFICATION

Please enter the following amendments to paragraphs **0011**, **0021**, **0022**, **0028**, **0032**, **0048**, **0050**, and **0053** of the specification:

[0011] The present invention relates to methods and catalyst systems for catalyzing enantioselective oxidation reactions, including enantioselective oxidation reactions of secondary alcohols and other similarly reactive organic substrates. The methods and catalyst systems described herein are particularly useful for kinetic resolution of racemic mixtures of enantiomers, for example secondary alcohols. As will be described in detail below, ~~greater than 99%~~
enantimeric excess of the unreacted alcohol can be achieved the invention can provide a single enantiomer at an enantiomeric excess of greater than 99% from a racemic mixture of enantiomers, e.g., secondary alcohols.

[0021] The term "~~ee~~" is terms "enantiomeric excess" and "ee" are intended to represent the percentage ~~obtained by of one enantiomer in a mixture of enantiomers.~~ For example, the enantiomeric excess of an R-enantiomer in a mixture of R- and S-enantiomers can be determined by subtracting the amount of the S-enantiomer from the R-enantiomer, and dividing by the sum of the amount of R-enantiomer and S-enantiomer[[:]].

[0022] The term "heteroatom" refers to nitrogen, oxygen, sulfur, phosphorus and silicon. As a linker, the heteroatom is represented by -O-, -S-, -NR-, etc. The heteroatoms can exist in any of their chemically allowed oxidation states. Thus a sulfur heteroatom can exist as be in the form of a sulfide, sulfoxide, or sulfone.

[0028] By selectively oxidizing a single enantiomer ~~when selectively oxidizing a compound enantiomer~~ according to the method of the invention, at least two products will be produced: the oxidized compound and the single enantiomer of the excess unreacted compound. In this reaction, ~~the percentage of enantiomer that consists of~~ a single enantiomer preferably is at least

about 50%, more preferably greater than 60% and most preferably greater than 90% of the unreacted compound.

[0032] The organic compound may be oxidized by contacting the organic compound with a catalyst system in a suitable organic solvent such as toluene, *tert*-amyl alcohol, ~~water~~, CHCl_3 , methylene chloride, 1,2-dichloroethane, and benzene. Other suitable solvents for oxidation reactions are well known in the art.

[0048] The oxidation of ethylene to acetaldehyde, commonly referred to as the Wacker oxidation reaction (Smidt et al., *Angew. Chem.* 71:176 (1959); Smidt et al., *Angew. Chem., Int. Ed. Engl.* 1:80 (1962); and Smidt, *J. Chem. Ind.* 54 (1962)), is one of the best-known reactions catalyzed by palladium(II). Typically, palladium is complexed with a copper co-oxidant to re-oxidize the palladium, such as $\text{PdCl}_2\text{-CuCl}_2$. This oxidation reaction is useful in the synthetic transformation of olefins, but there has been minimal work on catalyzed enantioselective Wacker-type cyclization reactions. See for example, Uozumi et al., *J. Org. Chem.* 63:5071-5075 (1998), where a ~~Pd-borax~~ a Pd-borax catalyst was used in combination with benzoquinone as the co-oxidant.

[0050] In one embodiment of the invention, the enantioselective oxidation reaction is an enantioselective aromatic oxidation reaction. This reaction typically involves the oxidation of a hydroxymethylphenol to a spiro epoxy-cyclohexadienone cyclohexadienone. Scheme IV illustrates one such reaction. It is understood however, that other compounds that undergo this type of reaction can be used instead of compound IV.1. For example, the compound can have one or more substitutions on the aromatic ring or the compound may be a heteroaryl or other aryl ring.

[0053] In addition to the reactions illustrated above as Schemes I-X, the catalyst system of the invention finds utility in the improved synthesis of numerous pharmaceutical agents that have chiral centers. Such pharmaceutical agents can thus exist as a ~~pair~~ mixture of enantiomers. When chemically synthesized, the resulting product is often a racemic mixture ~~so the two~~

~~enantiomers, and~~ in which typically only one enantiomer is optically active. Thus, the product must be resolved prior to use. This additional step is often lengthy and can involve loss of up to half of the material. Thus if these pharmaceutical agents could be synthesized by an enantioselective reaction, only the optically active enantiomer would be produced.